REMARKS

I. Claim Status

Claim 3 has been amended and claims 4 and 5 have been cancelled without prejudice to further prosecution in one or more related continuation or divisional applications. New claims 66-70 have been added. Support for the amendments and new claims can be found throughout the specification at, for example, page 25, lines 11-14, page 22, line 5, page 19, lines 24-25 (claim 3); page 23, lines 24-27 (claims 66 and 67); page 22, lines 28-33 (claims 68 and 29); and page 25, lines 1-6 (claim 70). Therefore, no new matter has been introduced by the subject amendments and new claims. Accordingly, claims 3, 6, 63, and 66-70 are pending and all read on the elected species.

II. Specification

The abstract of the disclosure has been objected to for the reason of it being the PCT abstract. No further explanation is provided. The abstract of this application published with the international application under PCT Article 21. Applicants' understanding is that use of a PCT abstract in national stage prosecution is not per se improper if that application published with the international application, and further that the abstract need not, in addition, be provided on a separate sheet. See Examiner Notes to MPEP § 608.01(b). Applicants respectfully request further specificity as to the grounds of the objection so that the appropriate correction can be made.

III. Rejection under 35 U.S.C. § 112, first paragraph

Claims 3-6, 15, 58 and 63 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The Examiner states as her basis for the rejection that "[t]here is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision the various claim components that satisfy the functional limitations of the claims". Office Action at pages 7-8. The Examiner mentions more specifically, the genus of cells, polynucleotide encoding a polypeptide variant, stop codons, and termination suppression agents.

In an effort to expedite prosecution, the claims have been amended to specify that the cells are eukaryotic cells, that the termination suppression agent is an aminoglycoside antibiotic, and that FACS is used to carry out the selection step in c).

As to the polynucleotide encoding a polypeptide variant, Applicants respectfully submit that the level of skill and knowledge in the art is such that those skilled in the art would know from the description provided by Applicant, that polynucleotides encoding any number of polypeptide variants could be used in the method. The degree of predictability within the claimed genus is high because the skilled person would expect expression of the polypeptide variant by following the steps described in the specification.

With regards to the Examiner's objection to the genus of stop codons, Applicants believe that no issue is raised by reference to this genus because it is described in the specification and is also well known in the art.

The Written Description Training Materials published by the USPTO on March 25, 2008 (Revision 1) provides guidance as to how claims should be evaluated for compliance to the Written Description requirement. Example 16 in particular addresses the situation of a process claim which refers to the use of a genus of compounds, where novelty resides in the process steps. The hypothetical claim is directed to a method of introducing a nucleic acid into the mitochondria of mammalian cells, comprising: (a) contacting a nucleic acid with a compound X to form a complex of said nucleic acid and compound X; (b) contacting mammalian cells with said complex; and (c) incubating said cells and said complex under certain conditions. The analysis indicates that the specification describes the structure of X and one nucleic acid, an actual reduction to practice of one species within the claimed genus, and the fact that X is a known compound. Based on these facts and the level of skill and knowledge in the art, it is concluded that the degree of predictability within the claimed genus is high and that the skilled person would recognize the inventor had possession of the claimed invention at the time of filing.

In the present application, Applicants have provided numerous examples of a first polynucleotide encoding a polypeptide variant and at least one stop codon (e.g., Example 2 (UAA/UGA and Protein C), Example 4 (UAA and Factor VII); Example 5 (UGA and Interferon α)).

Applicants respectfully submit that in view of the description provided in the specification, the skilled person would recognize that the genus of elements specified in each step of the claims is adequately described.

Accordingly, withdrawal of the written description rejections is respectfully requested.

IV. Rejection under 35 U.S.C. § 112, second paragraph

Claims 3-6, 15, 58, and 63 stand rejected under 35 U.S.C. § 112, second paragraph. These rejections are respectfully traversed.

The Examiner believes that there is insufficient antecedent basis for the limitations, "the presence of a termination suppression agent" in claim 3, step b), "the surface of said cell" in claim 6, and "the absence of a termination suppression agent" in claim 15. Applicants respectfully disagree. While Applicants appreciate that certain terms can be unclear where it is uncertain as to what element a limitation is referring to, Applicants do not believe that that situation presents itself in the limitations specified in this rejection. It is respectfully submitted that failure to provide explicit antecedent basis for terms does not always render a claim indefinite. A claim is not indefinite if the scope of the claim would be reasonably ascertainable by those skilled in the art. MPEP 2173.05(e), citing Energizer Holdings Inc. v. Int'l Trade Comm'n, 77 USPQ2d 1625 (Fed. Cir. 2006) and Ex parte Porter, 25 USPQ2d 144,1145 (Bd. Pat. App. & Inter. 1992). In this case, Applicants respectfully submit that the meaning of the terms "presence" and "absence" are clear. With respect to the limitation of "the surface of said cell", it is respectfully submitted that antecedent basis is provided in the recitation of "a plurality of eukaryotic cells" in step a). The "surface" is an inherent component of "cells" and does not require an antecedent recitation to "a surface of said at least one cell". MPEP § 2173.05(e) citing Bose Corp. v. JBL, Inc., 61 USPQ2d 1216, 1218-1219 (Fed. Cir. 2001).

In view of the above, withdrawal of the rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

V. Rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 102(e)

Claims 3, 6, and 15 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Light et al. (U.S. Pat. No. 5,770,356) and under 35 U.S.C. §102(e) as being allegedly anticipated by Ciceri et al. (U.S. publication 2007/0105093A1) These rejections are respectfully traversed.

Independent claim 3, from which all of the claims ultimately depend from, has been amended to specify that the termination suppression agent is an aminoglycoside antibiotic. Neither Light, et al., nor Ciceri, et al. describe the use of an aminoglycoside antibiotic during the cultivation of cells under conditions that allow expression of a polypeptide variant as claimed in step b). Accordingly, withdrawal of the rejections under 35 U.S.C. § 102 is respectfully requested.

VI. Rejection under § 103(a)

Claims 3-6, 15, 58 and 63 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ciceri or Light in view of Manuvakhova et al. (RNA, 100, 1044-55) and Sabbadini et al. (U.S. Pat. No. 7,183,105) and Nolan (WO 97/27212). This rejection is respectfully traversed.

The Light et al. patent describes expression of anchored and non-anchored soluble heterologous polypeptides from phage using a single vector in which nucleotide sequences are present for encoding: a) a suppressor tRNA gene capable of expressing a suppressor tRNA molecule; and b) an expression cassette for expressing a first and second heterologous polypeptide subunit. Col. 17, lines 29-37. The cassette is described as being designed to produce both subunits, one anchored to a phage membrane coat protein, and the other not anchored, i.e., soluble, through the regulation of a nonsense chain termination codon and a tRNA suppressor gene. Col. 17, lines 41-44. tRNA suppressor genes are described as being well known in the art, and preferred tRNA suppressor genes are identified as being supD, supE, supF, supG, and supP. Col. 18, lines 5-12.

The Ciceri et al. patent publication describes a method of conducting phage display that permits the uncoupling of the propagation of phage containing inserted sequences encoding heterologous polypeptides from the expression of the heterologous polypeptides. Ciceri et al. describe the use of a phage derived nucleic acid construct that comprises a nucleic acid molecule

encoding both a phage surface protein and a heterologous polypeptide with a termination codon inserted between the two sequences. Para. [0012] It reports that expression of the fusion protein requires suppression of premature termination of translation at the termination codon. Id. The publication states that use of a combination of a suppressor construct capable of conditionally expressing a suppressor tRNA and the phage derived nucleic acid construct permits the uncoupling of expression of the phage surface protein and a heterologous polypeptide such that the phage protein may be expressed without co-expression of the heterologous polypeptide as a fusion product with the phage protein. See para. [0018]

Both Light et al. and Ciceri et al. describe methods of expressing heterologous polypeptides on the surface of filamentous phage particles using a coat protein anchor that require the co-expression of a suppressor tRNA gene. The disclosures in these references differ from the subject matter claimed in the present application in several ways, for example, the fact that both references describe the use of amber suppressor tRNA rather than an aminoglycoside antibiotic, and the fact that both deal with expression on the surface of filamentous phage using a phage coat protein anchor, i.e., something entirely different from expression and selection of proteins from eukaryotic cells.

There is no disclosure or suggestion in either the Light et al. patent or the Ciceri et al. publication to perform the claimed method which requires, *inter alia*, the cultivation of eukaryotic cells in the presence of an aminoglycoside antibiotic and FACS. The Ciceri et al. reference further teaches away from claim element a) which requires the cell membrane anchoring peptide to be downstream of the at least one stop codon. In contrast, Ciceri et al. describe the advantage of their invention to be the fact that the coat protein can be expressed without expression of the heterologous protein, not vice-versa. Neither reference provides any motivation to deviate from the use of suppressor tRNA genes or phage display.

Addition of the Manuvakhova et al., Sabbadini et al., and Nolan references does nothing to render the claimed invention obvious. Manuvakhova et al. describe studies to determine whether the sequence context surrounding a stop codon can influence aminoglycoside-mediate suppression of translation termination signals in *in vitro* translational assays. No where does the Manuvakhova et

al. reference describe or suggest the use of an aminoglycoside in a method for screening or selecting a cell expressing a polypeptide with a desired binding affinity to a ligand, as claimed. The reference, however, does shed some light as to the motivation for the studies. Manuvakhova et al. state that "a pharmacological approach aimed at suppressing premature stop mutations may be applicable to common genetic diseases such as cystic fibrosis and muscular dystrophy." Page 1045, left column. The Sabbadini et al. reference is being cited for its disclosure of FACS analysis of isolated cells and the incorporation of GPI and other membrane-targeting elements in a fusion protein to direct the chimeric molecule to the cell surface. The Nolan reference is cited only for the proposition that phenotypic changes of cells can be sorted using FACS. None of the cited references provide any motivation for completely substituting the phage display system described in the Light et al. and Ciceri et al. references with a cell-based screening method which utilizes an aminoglycoside antibiotic.

In view of the above, it is respectfully submitted the claims are non-obvious over the cited references and withdrawal of this rejection is respectfully requested.

VII. Supplemental Information Disclosure Statement

Applicants wish to point out to the Examiner that a Supplemental Information Disclosure statement has been filed concurrently herewith.

CONCLUSION

In light of the foregoing, favorable action on all calims is earnestly solicited. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set forth below. The Commissioner is hereby authorized to charge any deficiency in fees or credit any overpayment to Deposit Account No. 50-0990. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 298-5308.

Respectfully submitted,

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